FACULTY OF PHARMACEUTICAL SCIENCES

infinity in vivo small animal imaging lab

Radiosynthesis and *in vivo* evaluation of [^{18}F] FABABA, a new ASCT-2 inhibitor.

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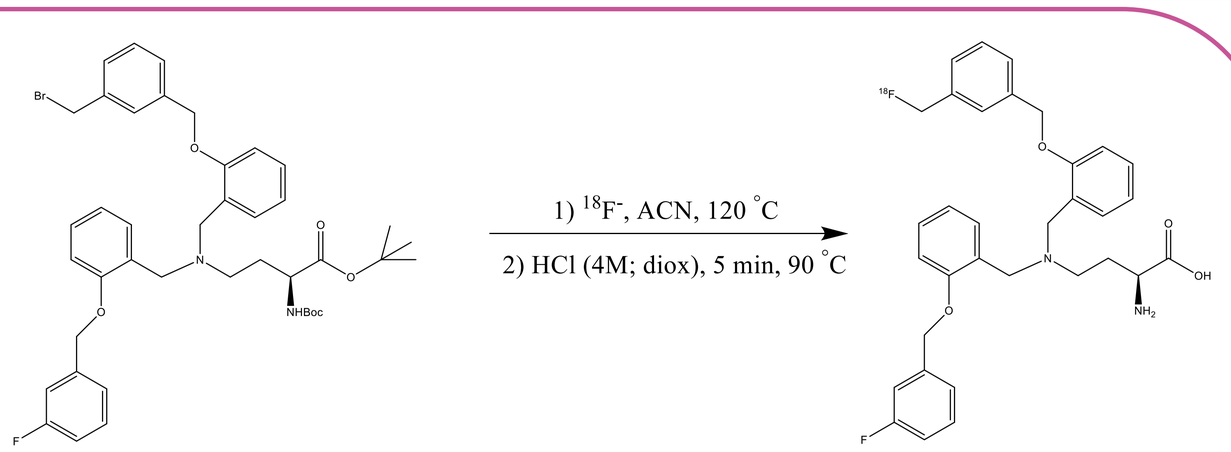
INTRODUCTION

Cancer is characterized by upregulation of nutrient transporters such as GLUT-1, LAT-1 and ASCT-2. [^{18}F] FDG is the golden standard in oncology metabolism imaging, however this tracer shows sub-optimal characteristics in several tumors (e.g. brain-, prostate-, colorectal cancer). In a search to address these drawbacks, a ^{18}F labeled inhibitor ([^{18}F] (S)-2-amino-4-((2-((3-fluorobenzyl)oxy)benzyl)(2-((3-(fluoromethyl)benzyl)oxy)benzyl)amino)butanoic acid) of ASCT-2 was developed.

MATERIALS & METHODS

- Radiosynthesis: Optimization ^{18}F labelling
  - Solvent
  - Temperature
  - Mass of the precursor
- *In vivo* testing
  - PC-3 xenograft (5 x 10^6 cells) (n=2).
  - Radiosynthesis 20 minutes in acetonitrile at 120°C.
  - Followed by deprotection with HCl (4M/dioxane) 5 minutes at 90°C.
  - Purification was done by means of semi-prep HPLC.
  - Final formulation: 20% EtOH/80% PBS mixture.
  - Dynamic µPET-scan acquired for 2 hours after injection of 18.5 MBq.
  - Volumes of interest are drawn around the tumor and the contralateral side as reference region with PMOD.



RESULTS

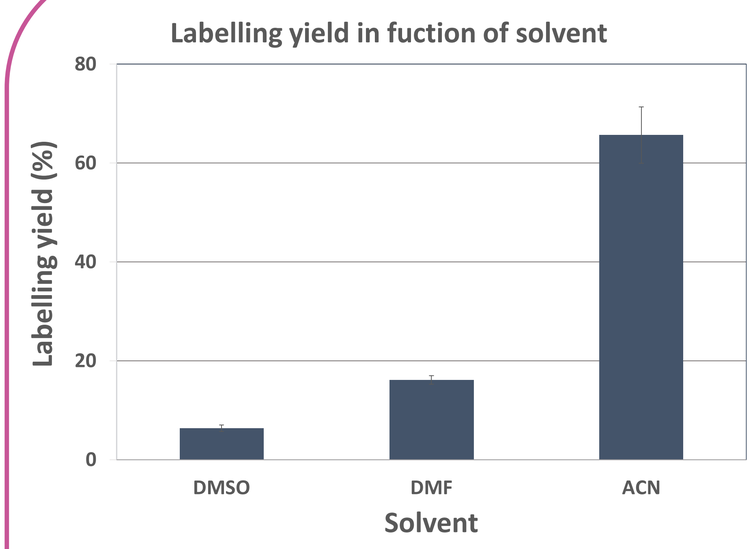


Figure 1: Labelling yield in function of different solvents. Altering the solvent to **acetonitrile** resulted in substantial increase in labelling yield.

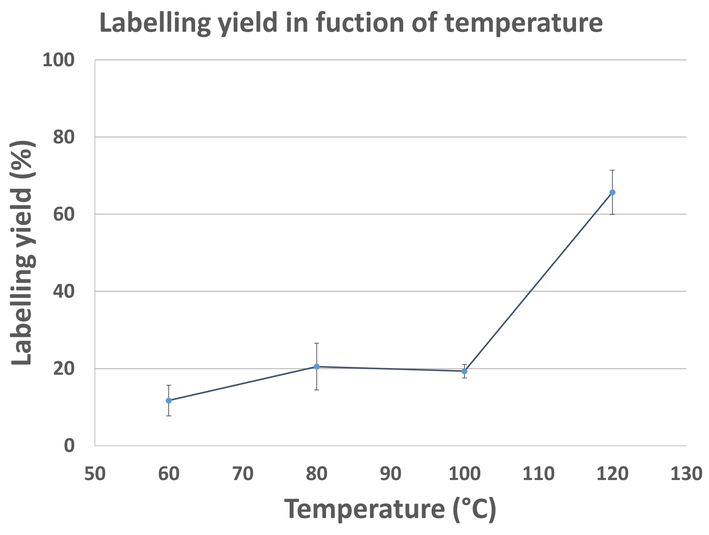


Figure 2: In the temperature-yield curve an inflection point is seen between 100°C and **120°C**, suggesting this accounts for the E_{kin} necessary for good labelling yields.

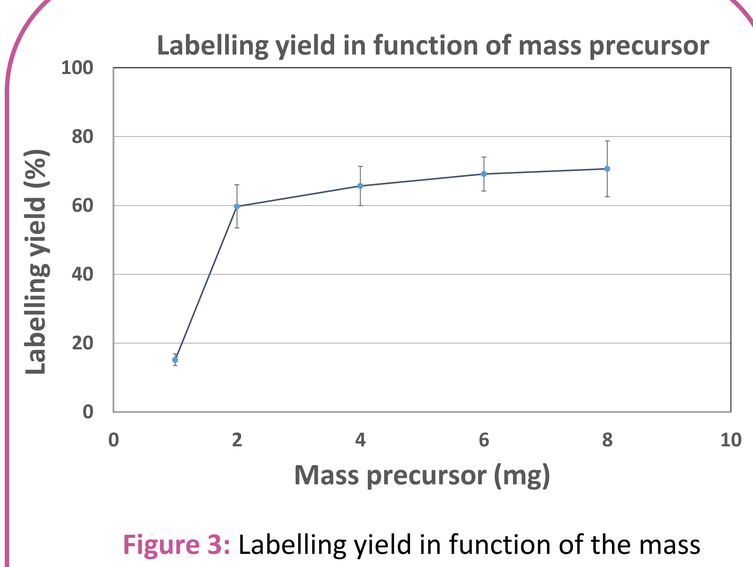


Figure 3: Labelling yield in function of the mass shows increase in yield at **2mg**. Increasing the amount of precursor further from 2mg to 8mg did not increase the labelling yield significantly.

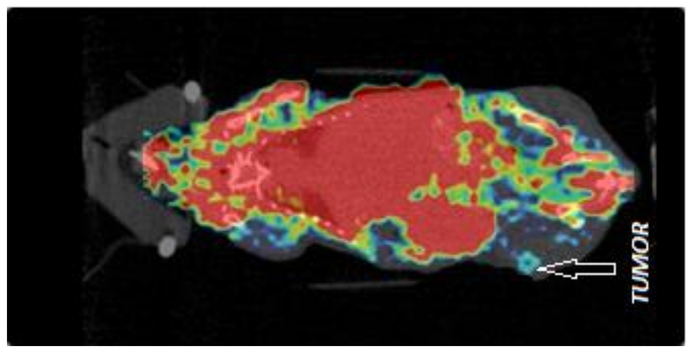


Figure 4: µPET/CT image of PC-3 xenograft.
The tracer shows *in vivo* uptake in the tumor and makes a clear delineation of the tumor possible. Furthermore it is predominantly cleared via biliary transport and in a minor amount to the bladder.
The tracer reports an optimal uptake in the tumor after 20 minutes and an average **tumor to background ratio of 1.85 ± 0,13 (n=2)**.

CONCLUSIONS

With this study we report a new radiolabeled inhibitor of ASCT-2, which shows a good TBR. Further experiments are needed to explore the imaging potential of the ASCT-2 transporter. Optimal labelling conditions are also reported which suggest the labelling should occur in acetonitrile with a temperature of 120°C.

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